Figure 1

Nucleotide sequence for 1068 heavy chain variable region

ATGGGATGGAGCTATATCATCCTCTTTTTGGTAGCAACAGCTACAGATGTCCACTCCCAGGTCCA
ACTGCAGCAGCCTGGGGCTGAACTGGTGCAGCCTGGGACTTCAGTGAGGCTGTCCTGCAAGGCTT
CTGGCTACATCTTCACCACCTACTGGATTCACTGGGTGAAACAGAGGCCTGGACAGGGCCTTGAG
TGGATTGGAGAGATTAACCCTAACAACGGTCGTATTAACTACAATGAGAAATTCAAGACCAAGGC
CACACTGACTGTAGACAAATCCTCCAGCACAGCCTACATGCAACTCAGCAGCCTGACATCTGAGG
ACTCTGCGGTCTATTACTGTACAAGAGTAGGGGTTATGATTACGACGTTTCCTTACTGGGGCCAA
GGGACTCTGGTCACTGTCTCTGCA (SEQ ID NO: 5)

Amino Acid sequence for 1068 heavy chain variable region

MGWSYIILFLVATATDVHSQVQLQQPGAELVQPGTSVRLSCKASGYIFTTYWIHWVKQRPGQGLE
WIGEINPNNGRINYNEKFKTKATLTVDKSSSTAYMQLSSLTSEDSAVYYCTRVGVMITTFPYWGQ
GTLVTVSA (SEQ ID NO: 6)

Signal Sequence

MGWSYIILFLVATATDVHS (SEQ ID NO: 7)

FR1

QVQLQQPGAELVQPGTSVRLSCKASGYIF (SEQ ID NO: 8)

CDR1

TTYWIH (SEQ ID NO: 9)

FR2

WVKQRPGQGLEWIG (SEQ ID NO: 10)

CDR2

EINPNNGRINYNEKFKT (SEQ ID NO: 11)

FR3

KATLTVDKSSSTAYMQLSSLTSEDSAVYYCTR (SEQ ID NO: 12)

CDR3

VGVMITTFPY (SEQ ID NO: 13)

FR4

WGQGTLVTVSA (SEQ ID NO: 14)

Figure 2

Nucleotide sequence for 1068 light chain variable region

ATGAGTGTGCTCACTCAGGTCCTGGCGTTGCTGCTGCTGTGGCTTACAGGTGCCAGATGTGACAT
CCAGATGACTCAGTCTCCAGCCTCCCTATCTGCATCTGTGGGAGAAACTGTCACCATCACATGTC
GAGCAAGTGGGAATATTCACAATTATTTAGCATGGTATCAGCAGAAACAGGGAAAATCTCCTCAG
CTCCTGGTCTATAATGCAAAAACCTTAGCAGATGGTGTGCCATCAAGATTCAGTGGCAGTGAATC
AGGAACACAATATTCTCTCAAGATCAACAGCCTGCAGCCTGAAGATTTTGGGAGTTATTACTGTC
AACATTTTTGGAGTACTCCATTTACGTTCGGCTCGGGGACAAAGTTGGAACTAAAA (SEQ ID
NO: 15)

Amino Acid sequence for 1068 light chain variable region

MSVLTQVLALLLLWLTGARCDIQMTQSPASLSASVGETVTITCRASGNIHNYLAWYQQKQGKSPQ
LLVYNAKTLADGVPSRFSGSESGTQYSLKINSLQPEDFGSYYCQHFWSTPFTFGSGTKLELK
(SEQ ID NO: 16)

Signal sequence

MSVLTQVLALLLLWLTGARC (SEQ ID NO: 17)

FR1

DIQMTQSPASLSASVGETVTITC (SEQ ID NO: 18)

CDR1

RASGNIHNYLA (SEQ ID NO: 19)

FR2

WYQQKQGKSPQLLVY (SEQ ID NO: 20)

CDR2

NAKTLAD (SEQ ID NO: 21)

FR3

GVPSRFSGSESGTQYSLKINSLQPEDFGSYYC (SEQ ID NO: 22)

CDR3

QHFWSTP (SEQ ID NO: 23)

FR4

FTFGSGTKLELK (SEQ ID NO: 24)

Figure 3

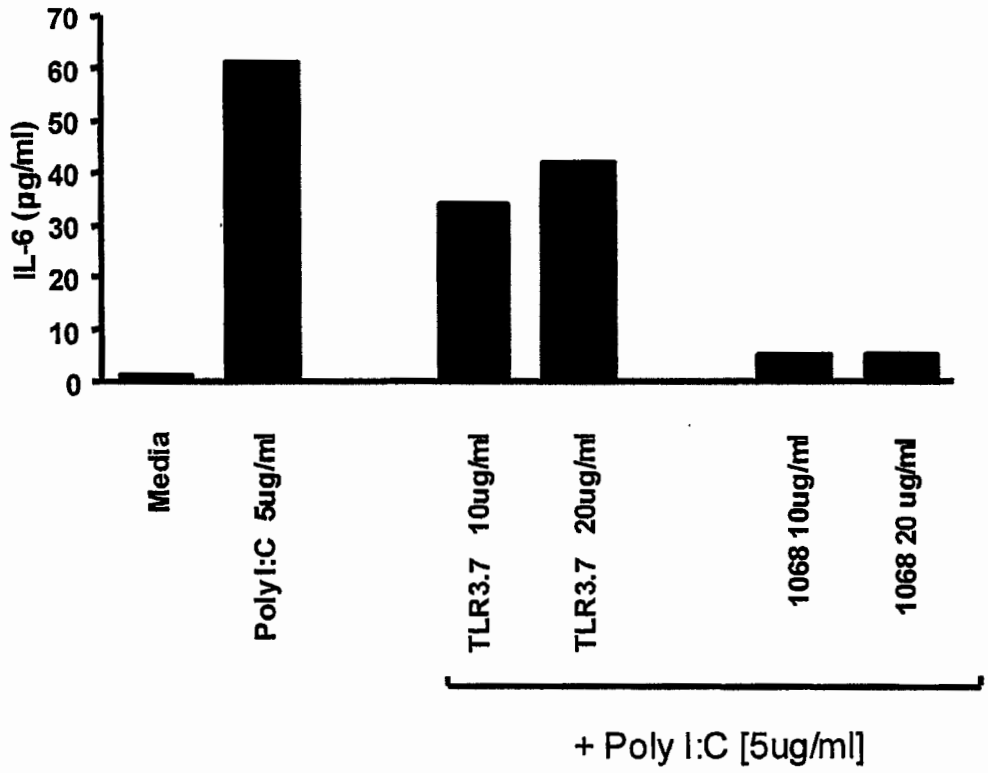

70
60
50
40
30
20
10
0
IL-6 (pg/ml)
Media
Poly I:C 5ug/ml
TLR3.7 10ug/ml
TLR3.7 20ug/ml
1068 10ug/ml
1068 20 ug/ml
+ Poly I:C [5ug/ml]

Figure 4

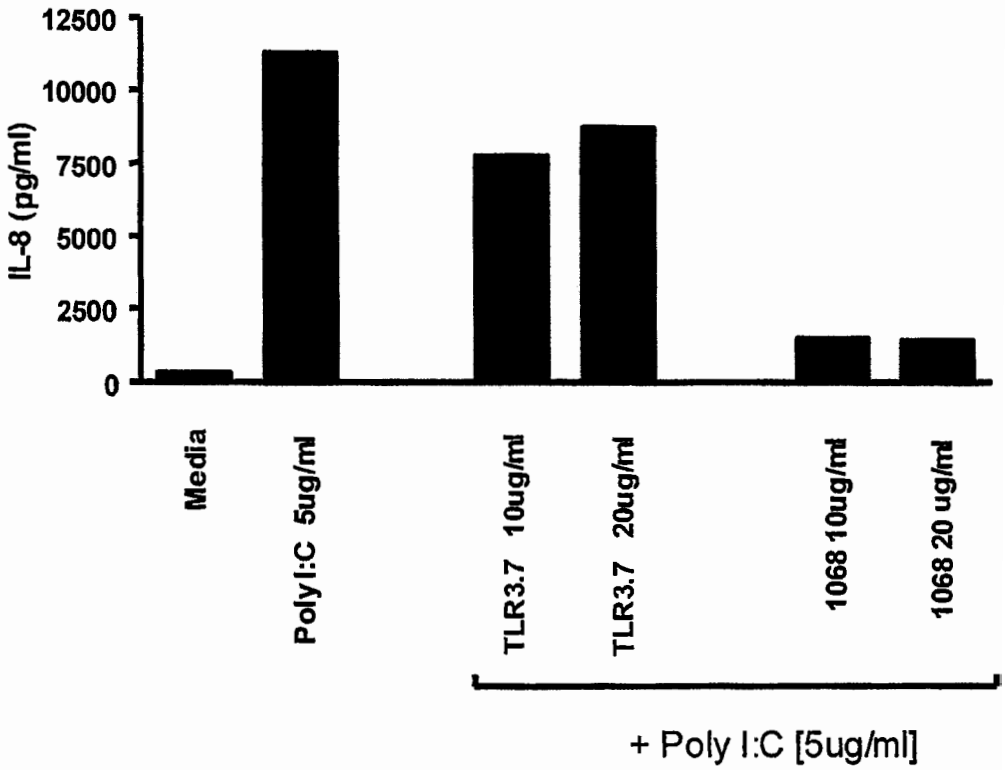

12500
10000
7500
5000
2500
0
IL-8 (pg/ml)
Media
Poly I:C 5ug/ml
TLR3.7 10ug/ml
TLR3.7 20ug/ml
1068 10ug/ml
1068 20 ug/ml
+ Poly I:C [5ug/ml]

Figure 5

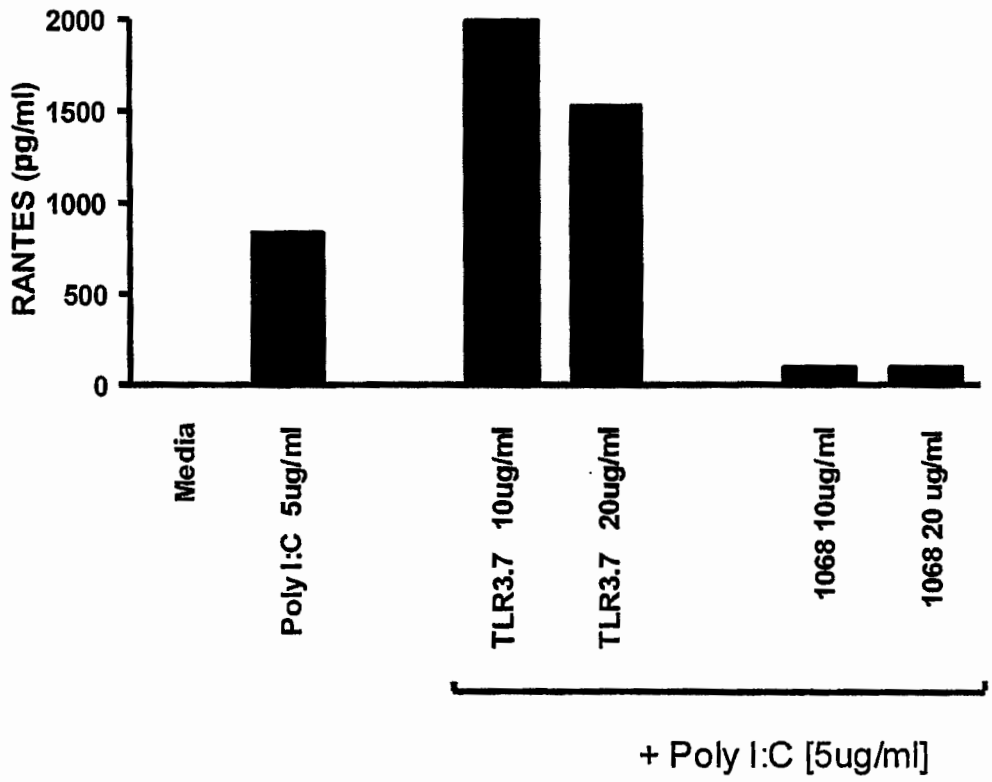

2000
1500
1000
500
0
RANTES (pg/ml)
Media
Poly I:C 5ug/ml
TLR3.7 10ug/ml
TLR3.7 20ug/ml
1068 10ug/ml
1068 20 ug/ml
+ Poly I:C [5ug/ml]

Figure 6

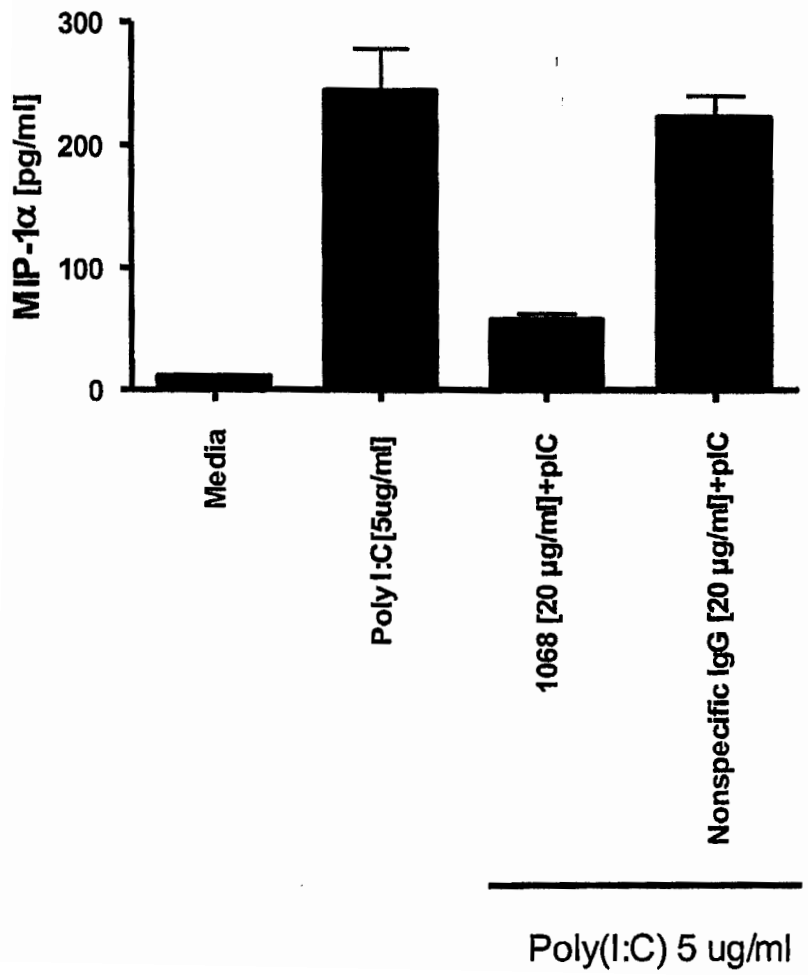

MIP-1α [pg/ml]
300
200
100
0
Media
Poly I:C[5ug/ml]
1068 [20 µg/ml]+pIC
Nonspecific IgG [20 µg/ml]+pIC
Poly(I:C) 5 ug/ml

Figure 7

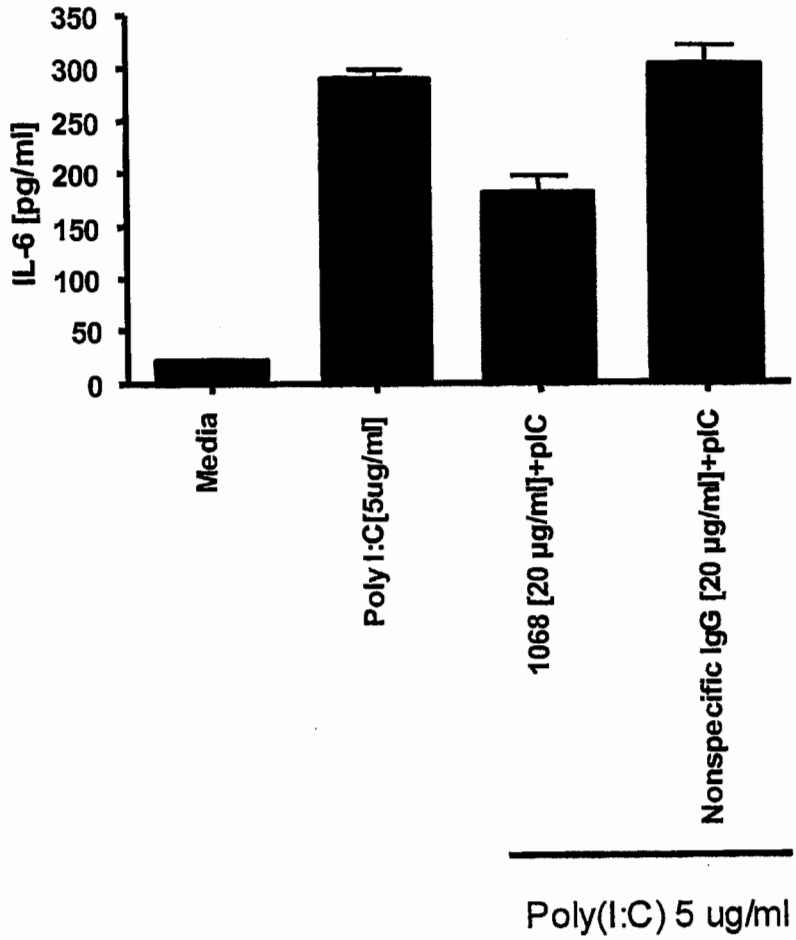

350
300
250
200
150
100
50
0
IL-6 [pg/ml]
Media
Poly I:C[5ug/ml]
1068 [20 µg/ml]+pIC
Nonspecific IgG [20 µg/ml]+pIC
Poly(I:C) 5 ug/ml

Figure 8

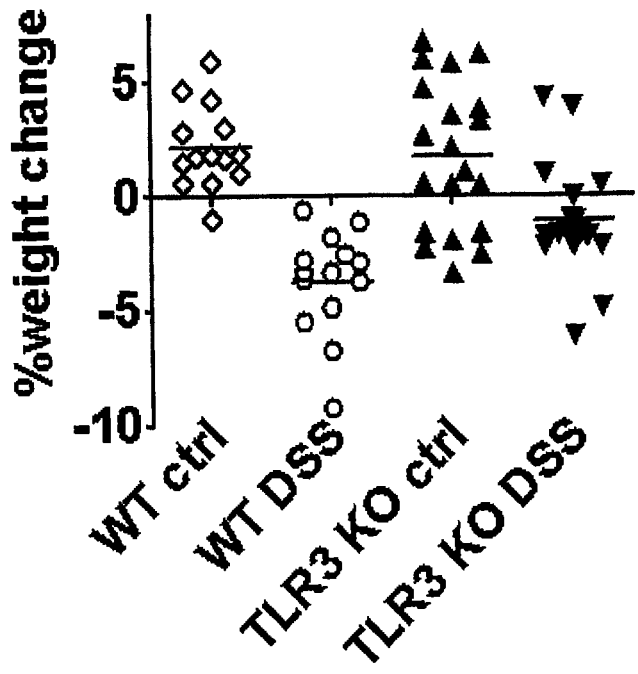


Figure 9

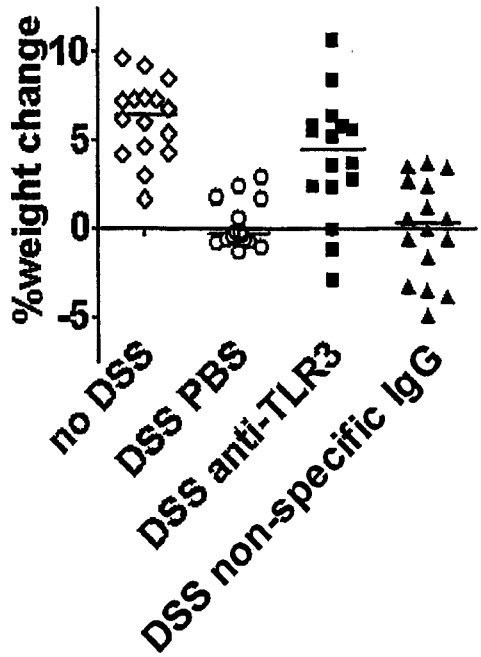

%weight change
10
5
0
-5
no DSS
DSS PBS
DSS anti-TLR3
DSS non-specific IgG

Figure 10

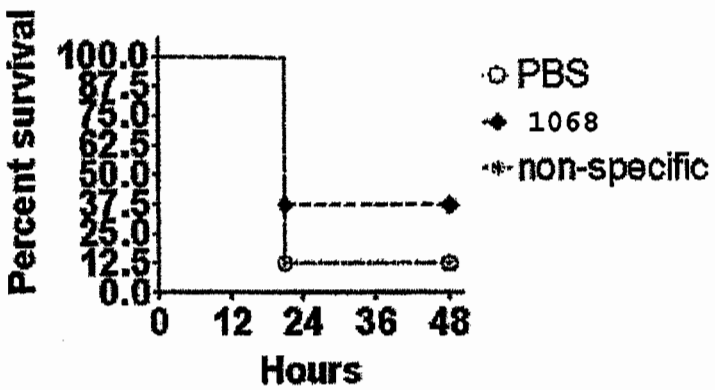

Percent survival
100.0
87.5
75.0
62.5
50.0
37.5
25.0
12.5
0.0
0
12
24
36
48
Hours
PBS
1068
non-specific

Figure 11

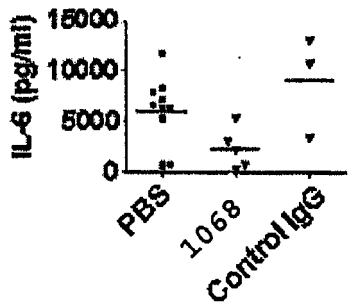


Figure 12

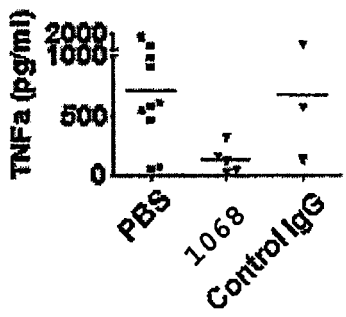


Figure 13

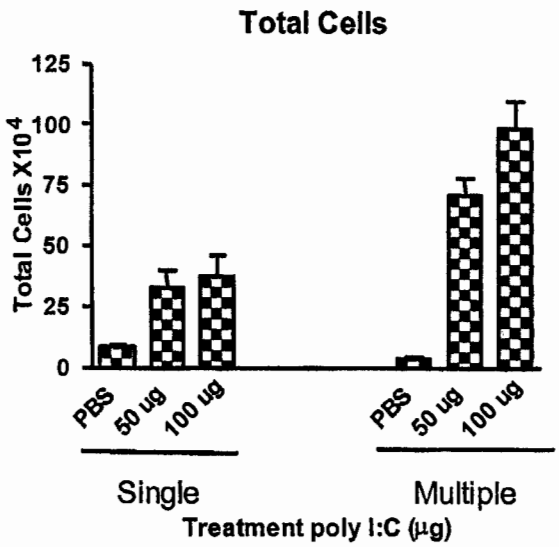

Total Cells
125
100
75
50
25
0
Total Cells X10^4
PBS
50 ug
100 ug
PBS
50 ug
100 ug
Single
Multiple
Treatment poly I:C (µg)

Figure 14

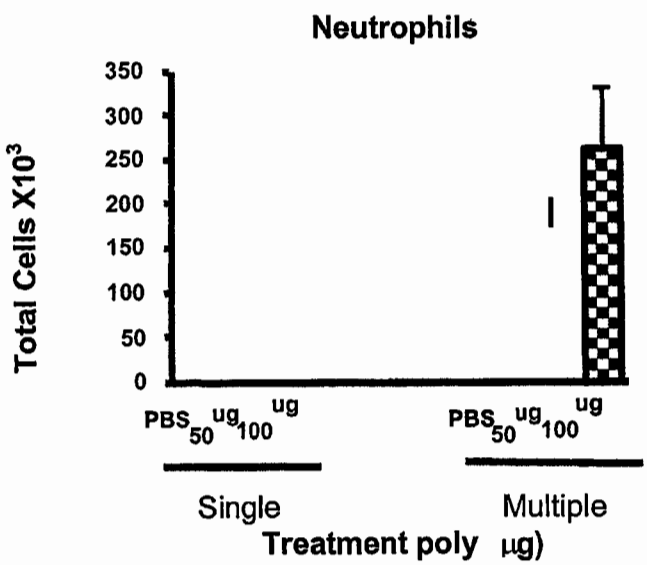

Neutrophils
Total Cells X10³
350
300
250
200
150
100
50
0
PBS
50 ug
100 ug
PBS
50 ug
100 ug
Single
Multiple
Treatment poly μg)

Figure 15

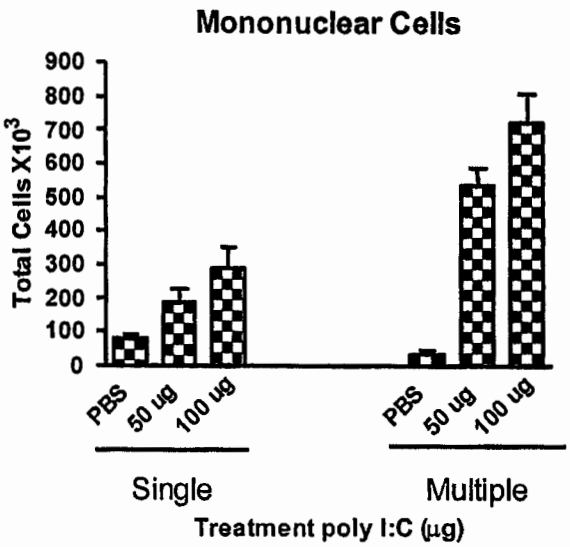

Mononuclear Cells
Total Cells X10^3
900
800
700
600
500
400
300
200
100
0
PBS
50 ug
100 ug
PBS
50 ug
100 ug
Single
Multiple
Treatment poly I:C (μg)

Figure 16

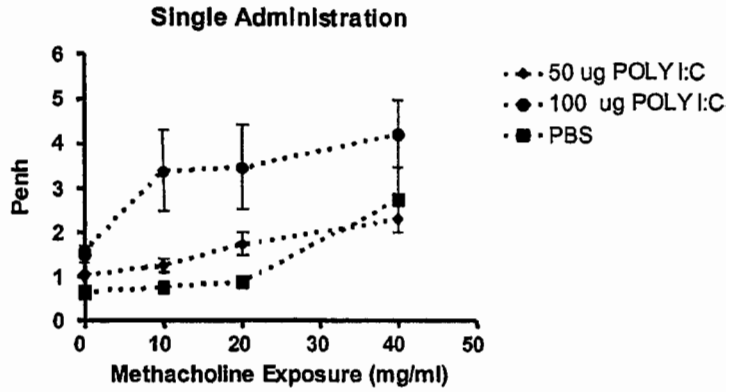

Single Administration
Penh
6
5
4
3
2
1
0
0
10
20
30
40
50
Methacholine Exposure (mg/ml)
50 ug POLY I:C
100 ug POLY I:C
PBS

Figure 17

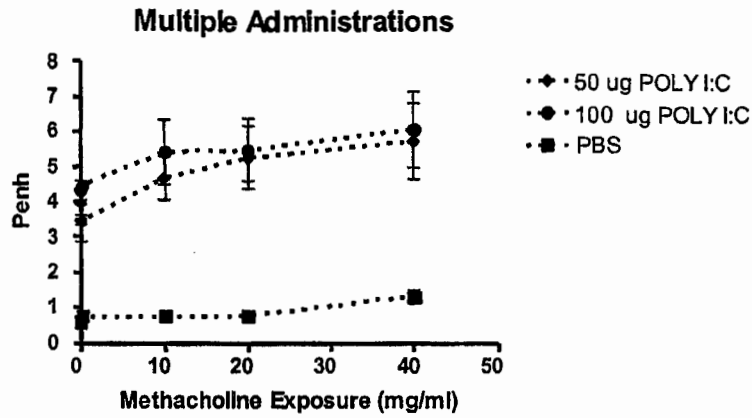

Multiple Administrations
Penh
8
7
6
5
4
3
2
1
0
0
10
20
30
40
50
Methacholine Exposure (mg/ml)
50 ug POLY I:C
100 ug POLY I:C
PBS

Figure 18

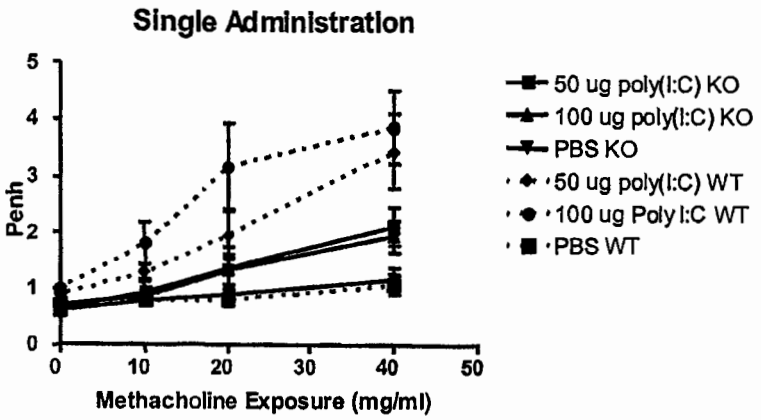

Single Administration
Penh
Methacholine Exposure (mg/ml)
0
1
2
3
4
5
0
10
20
30
40
50
50 ug poly(I:C) KO
100 ug poly(I:C) KO
PBS KO
50 ug poly(I:C) WT
100 ug Poly I:C WT
PBS WT

Figure 19

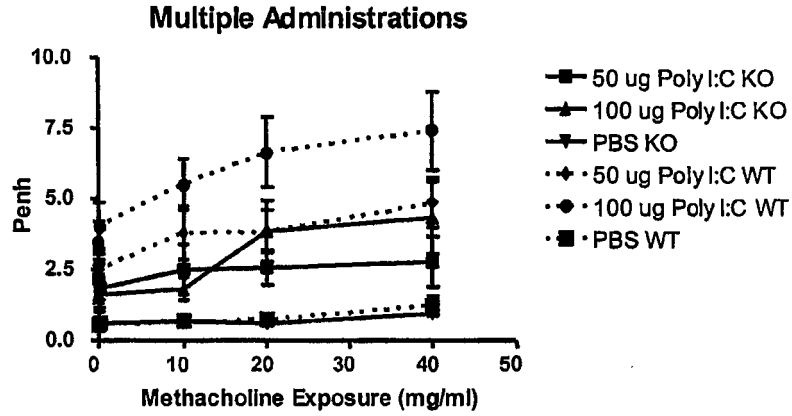

Multiple Administrations
10.0
7.5
5.0
2.5
0.0
Penh
0
10
20
30
40
50
Methacholine Exposure (mg/ml)
50 ug Poly I:C KO
100 ug Poly I:C KO
PBS KO
50 ug Poly I:C WT
100 ug Poly I:C WT
PBS WT

Figure 20

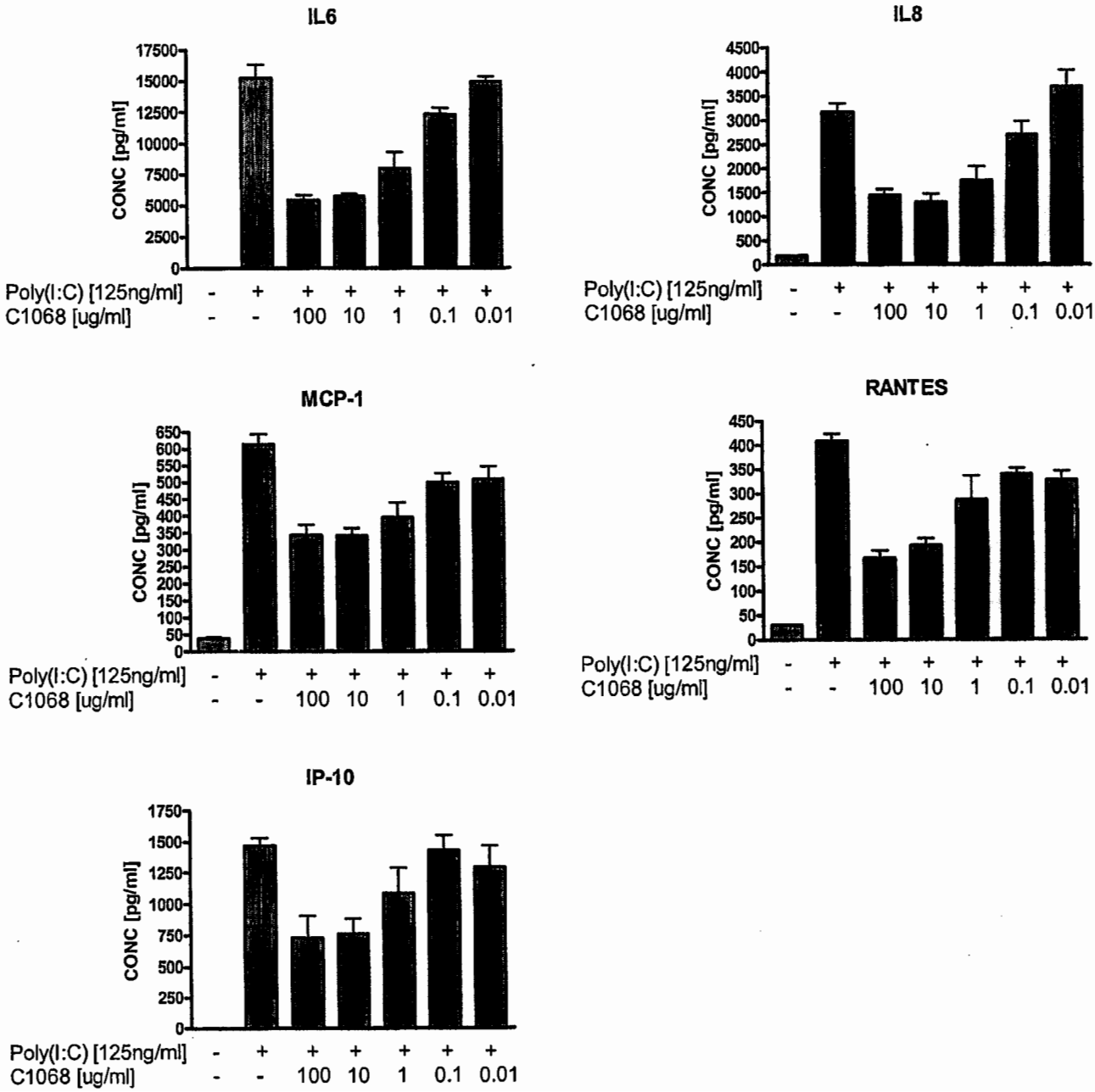

IL6
CONC [pg/ml]
17500
15000
12500
10000
7500
5000
2500
0
Poly(I:C) [125ng/ml] - + + + + + +
C1068 [ug/ml] - - 100 10 1 0.1 0.01
IL8
CONC [pg/ml]
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Poly(I:C) [125ng/ml] - + + + + + +
C1068 [ug/ml] - - 100 10 1 0.1 0.01
MCP-1
CONC [pg/ml]
650
600
550
500
450
400
350
300
250
200
150
100
50
0
Poly(I:C) [125ng/ml] - + + + + + +
C1068 [ug/ml] - - 100 10 1 0.1 0.01
RANTES
CONC [pg/ml]
450
400
350
300
250
200
150
100
50
0
Poly(I:C) [125ng/ml] - + + + + + +
C1068 [ug/ml] - - 100 10 1 0.1 0.01
IP-10
CONC [pg/ml]
1750
1500
1250
1000
750
500
250
0
Poly(I:C) [125ng/ml] - + + + + + +
C1068 [ug/ml] - - 100 10 1 0.1 0.01

Figure 21

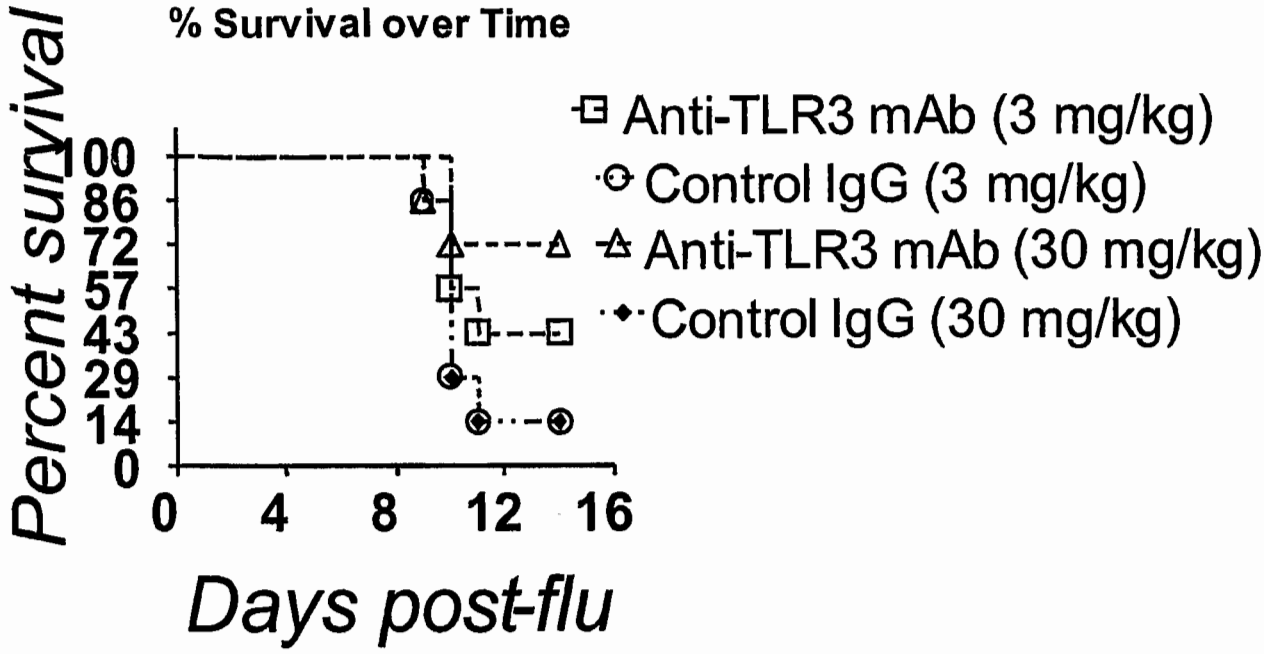

% Survival over Time
Anti-TLR3 mAb (3 mg/kg)
Control IgG (3 mg/kg)
Anti-TLR3 mAb (30 mg/kg)
Control IgG (30 mg/kg)
Percent survival
100
86
72
57
43
29
14
0
0
4
8
12
16
Days post-flu

Figure 22

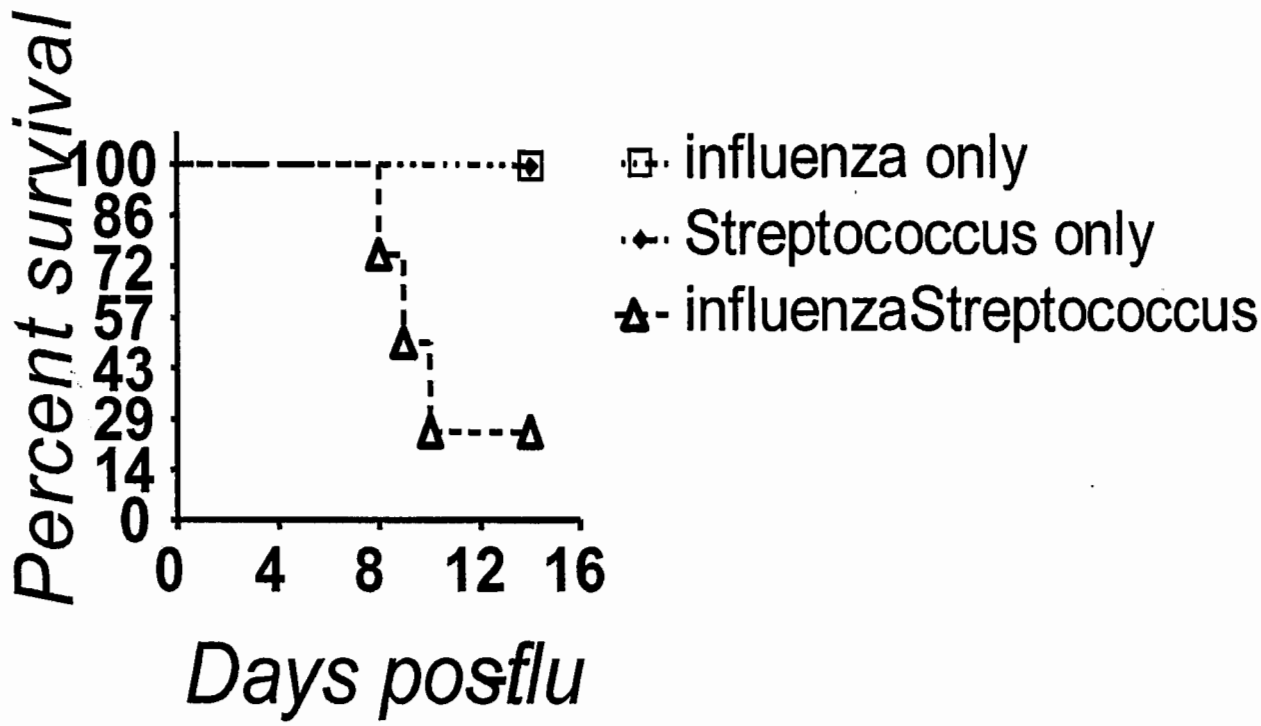

Percent survival
100
86
72
57
43
29
14
0
0
4
8
12
16
Days posflu
influenza only
Streptococcus only
influenzaStreptococcus

Figure 23

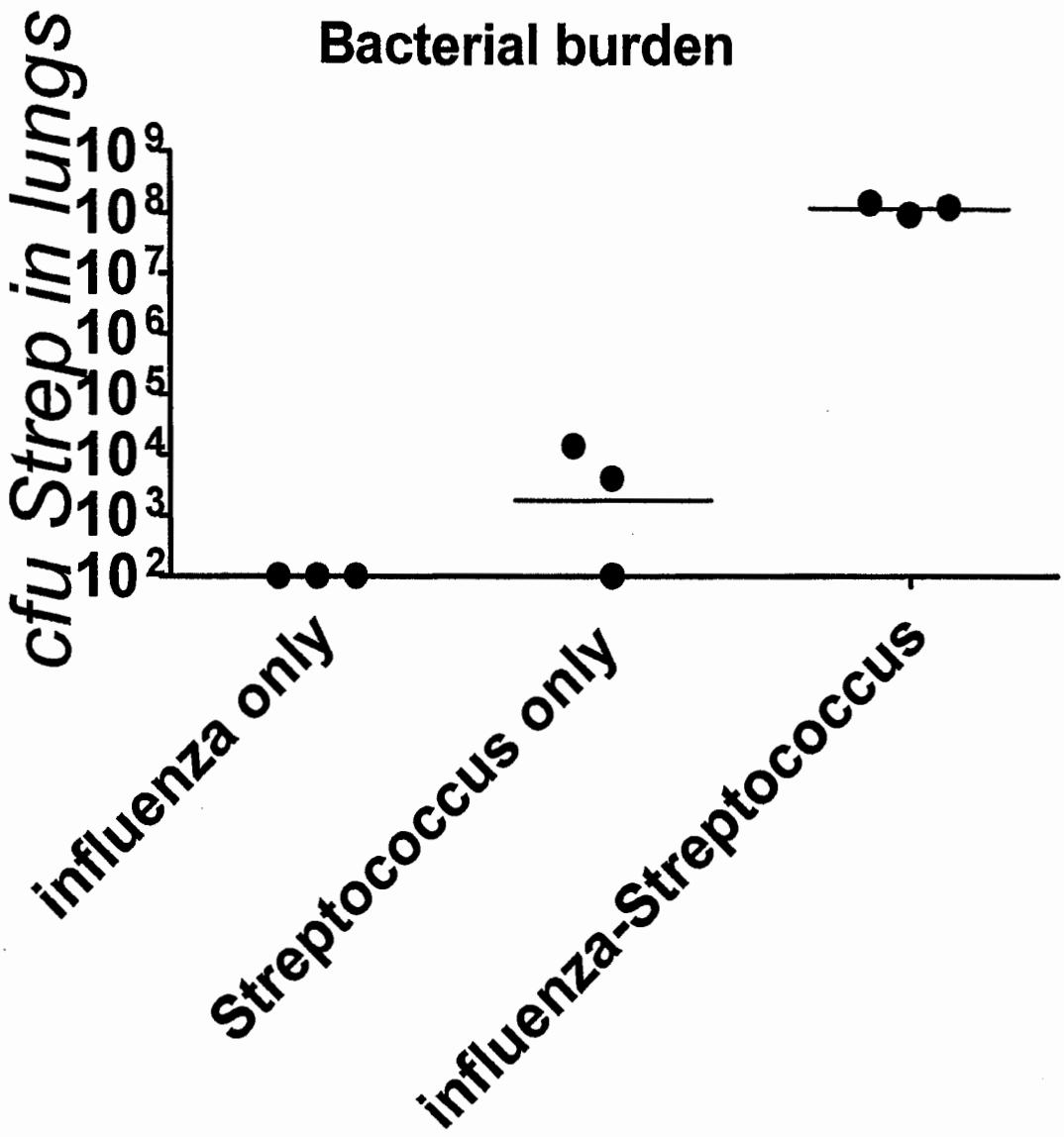

Bacterial burden
cfu Strep in lungs
10 9
10 8
10 7
10 6
10 5
10 4
10 3
10 2
influenza only
Streptococcus only
influenza-Streptococcus

Figure 24A

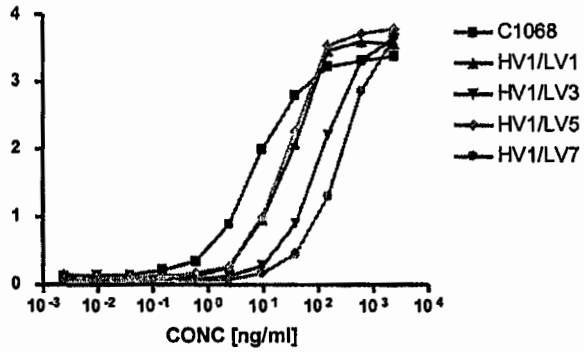


Figure 24B

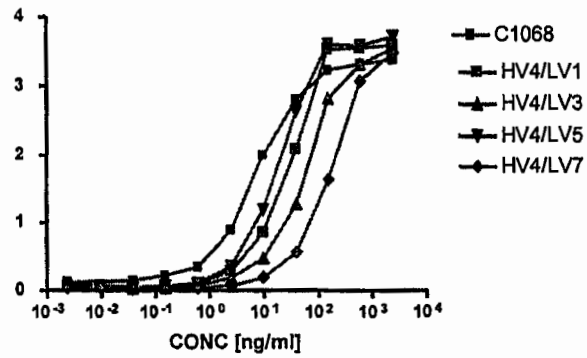


Figure 24C

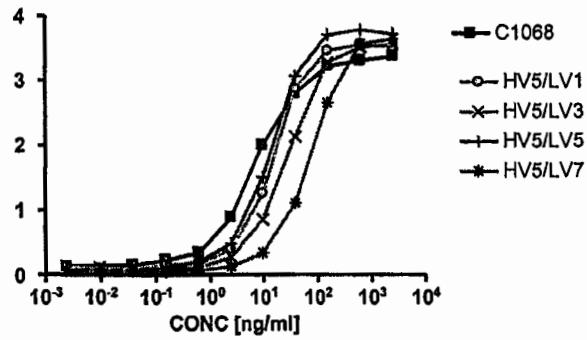


Figure 24D

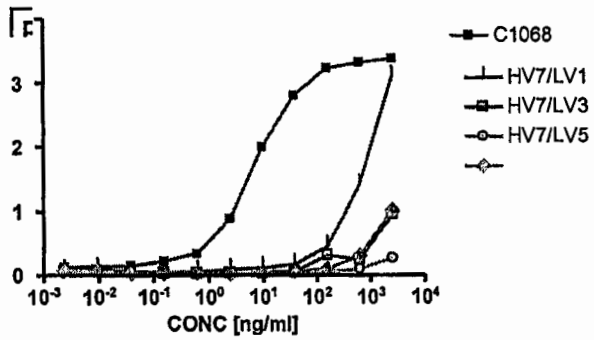


Figure 25

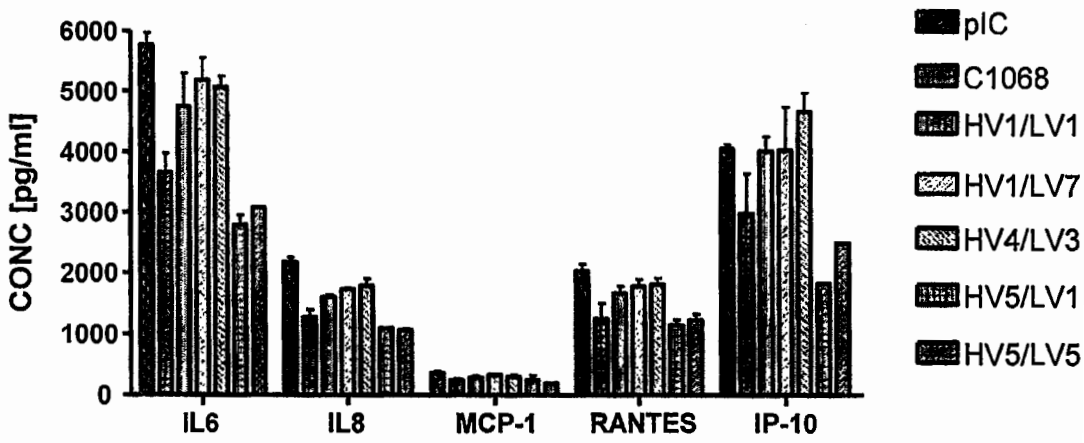

6000
5000
4000
3000
2000
1000
0
CONC [pg/ml]
IL6
IL8
MCP-1
RANTES
IP-10
pIC
C1068
HV1/LV1
HV1/LV7
HV4/LV3
HV5/LV1
HV5/LV5

Figure 26

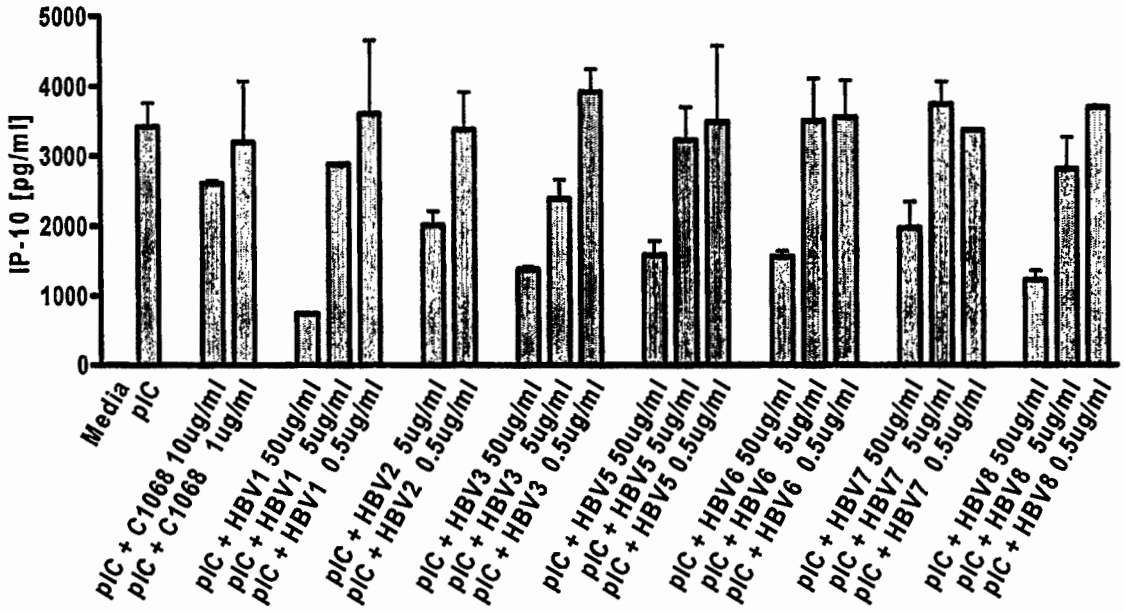

IP-10 [pg/ml]
5000
4000
3000
2000
1000
0
Media
pIC
pIC + C1068 10ug/ml
pIC + C1068 1ug/ml
pIC + HBV1 50ug/ml
pIC + HBV1 5ug/ml
pIC + HBV1 0.5ug/ml
pIC + HBV2 5ug/ml
pIC + HBV2 0.5ug/ml
pIC + HBV3 50ug/ml
pIC + HBV3 5ug/ml
pIC + HBV3 0.5ug/ml
pIC + HBV5 50ug/ml
pIC + HBV5 5ug/ml
pIC + HBV5 0.5ug/ml
pIC + HBV6 50ug/ml
pIC + HBV6 5ug/ml
pIC + HBV6 0.5ug/ml
pIC + HBV7 50ug/ml
pIC + HBV7 5ug/ml
pIC + HBV7 0.5ug/ml
pIC + HBV8 50ug/ml
pIC + HBV8 5ug/ml
pIC + HBV8 0.5ug/ml

Figure 27

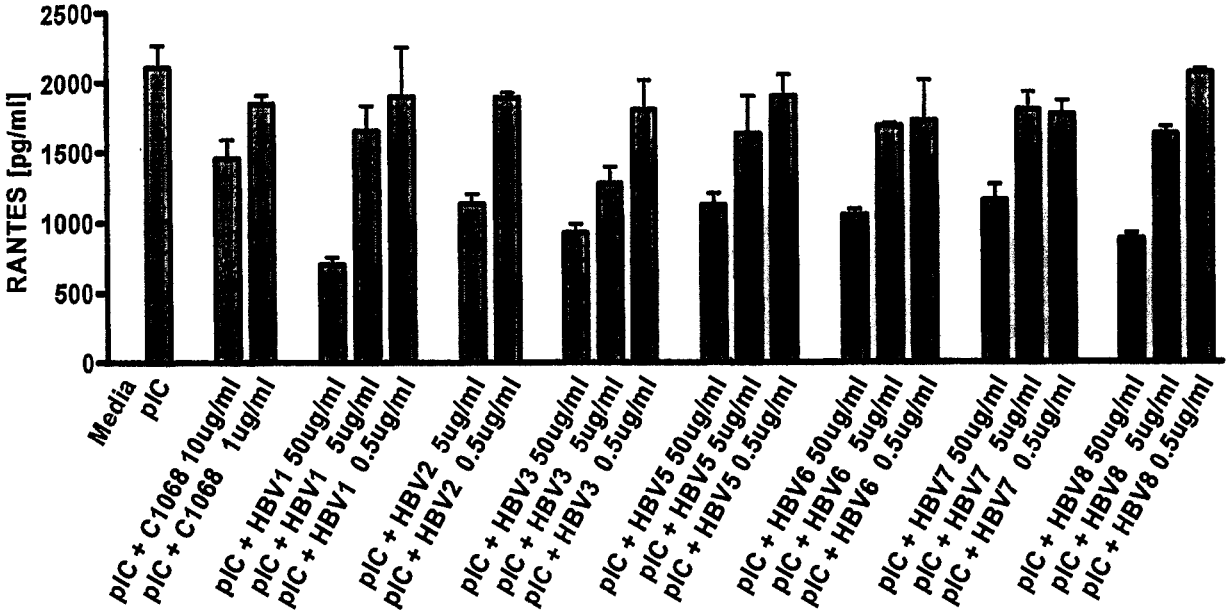

RANTES [pg/ml]
2500
2000
1500
1000
500
0
Media
pIC
pIC + C1068 10ug/ml
pIC + C1068 1ug/ml
pIC + HBV1 50ug/ml
pIC + HBV1 5ug/ml
pIC + HBV1 0.5ug/ml
pIC + HBV2 5ug/ml
pIC + HBV2 0.5ug/ml
pIC + HBV3 50ug/ml
pIC + HBV3 5ug/ml
pIC + HBV3 0.5ug/ml
pIC + HBV5 50ug/ml
pIC + HBV5 5ug/ml
pIC + HBV5 0.5ug/ml
pIC + HBV6 50ug/ml
pIC + HBV6 5ug/ml
pIC + HBV6 0.5ug/ml
pIC + HBV7 50ug/ml
pIC + HBV7 5ug/ml
pIC + HBV7 0.5ug/ml
pIC + HBV8 50ug/ml
pIC + HBV8 5ug/ml
pIC + HBV8 0.5ug/ml

Figure 28

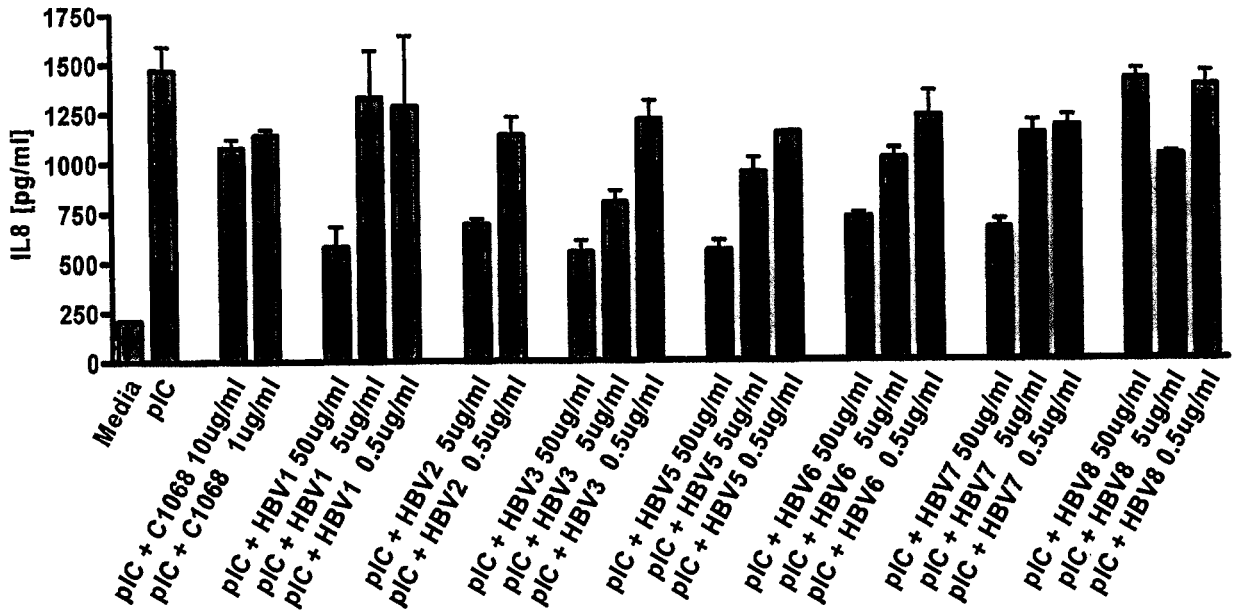

IL8 [pg/ml]
1750
1500
1250
1000
750
500
250
0
Media
pIC
pIC + C1068 10ug/ml
pIC + C1068 1ug/ml
pIC + HBV1 50ug/ml
pIC + HBV1 5ug/ml
pIC + HBV1 0.5ug/ml
pIC + HBV2 5ug/ml
pIC + HBV2 0.5ug/ml
pIC + HBV3 50ug/ml
pIC + HBV3 5ug/ml
pIC + HBV3 0.5ug/ml
pIC + HBV5 50ug/ml
pIC + HBV5 5ug/ml
pIC + HBV5 0.5ug/ml
pIC + HBV6 50ug/ml
pIC + HBV6 5ug/ml
pIC + HBV6 0.5ug/ml
pIC + HBV7 50ug/ml
pIC + HBV7 5ug/ml
pIC + HBV7 0.5ug/ml
pIC + HBV8 50ug/ml
pIC + HBV8 5ug/ml
pIC + HBV8 0.5ug/ml

Figure 29

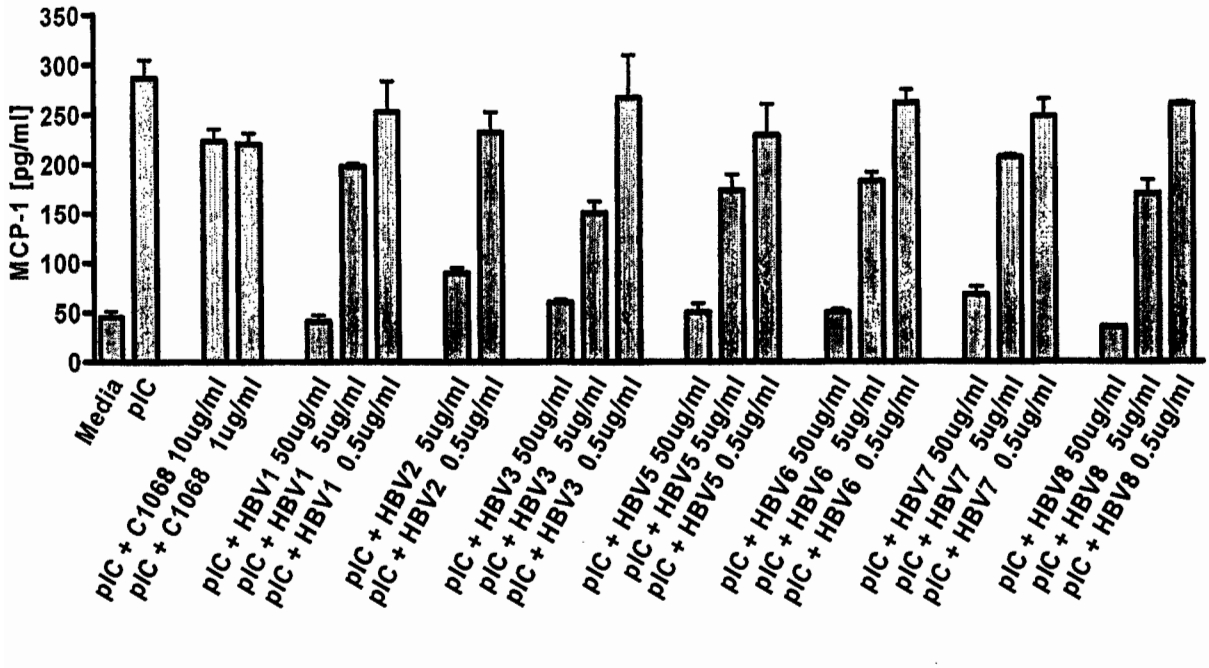

MCP-1 [pg/ml]
350
300
250
200
150
100
50
0
Media
pIC
pIC + C1068 10ug/ml
pIC + C1068 1ug/ml
pIC + HBV1 50ug/ml
pIC + HBV1 5ug/ml
pIC + HBV1 0.5ug/ml
pIC + HBV2 5ug/ml
pIC + HBV2 0.5ug/ml
pIC + HBV3 50ug/ml
pIC + HBV3 5ug/ml
pIC + HBV3 0.5ug/ml
pIC + HBV5 50ug/ml
pIC + HBV5 5ug/ml
pIC + HBV5 0.5ug/ml
pIC + HBV6 50ug/ml
pIC + HBV6 5ug/ml
pIC + HBV6 0.5ug/ml
pIC + HBV7 50ug/ml
pIC + HBV7 5ug/ml
pIC + HBV7 0.5ug/ml
pIC + HBV8 50ug/ml
pIC + HBV8 5ug/ml
pIC + HBV8 0.5ug/ml

Figure 30

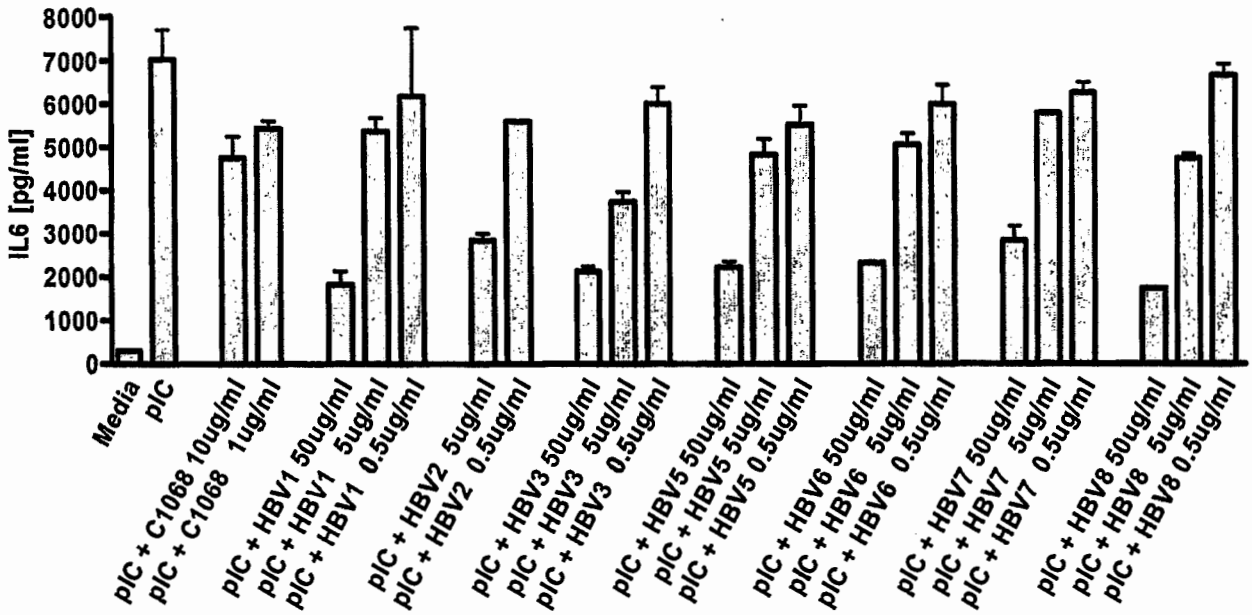

IL6 [pg/ml]
8000
7000
6000
5000
4000
3000
2000
1000
0
Media
pIC
pIC + C1068 10ug/ml
pIC + C1068 1ug/ml
pIC + HBV1 50ug/ml
pIC + HBV1 5ug/ml
pIC + HBV1 0.5ug/ml
pIC + HBV2 5ug/ml
pIC + HBV2 0.5ug/ml
pIC + HBV3 50ug/ml
pIC + HBV3 5ug/ml
pIC + HBV3 0.5ug/ml
pIC + HBV5 50ug/ml
pIC + HBV5 5ug/ml
pIC + HBV5 0.5ug/ml
pIC + HBV6 50ug/ml
pIC + HBV6 5ug/ml
pIC + HBV6 0.5ug/ml
pIC + HBV7 50ug/ml
pIC + HBV7 5ug/ml
pIC + HBV7 0.5ug/ml
pIC + HBV8 50ug/ml
pIC + HBV8 5ug/ml
pIC + HBV8 0.5ug/ml

Figure 31A

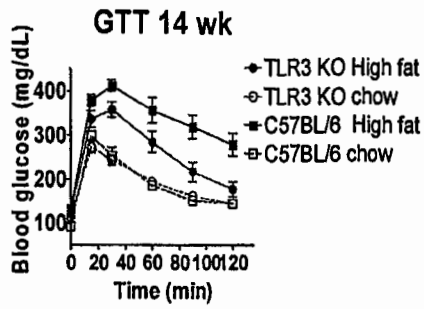


Figure 31B

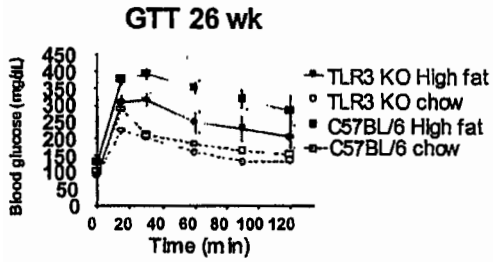


Figure 32

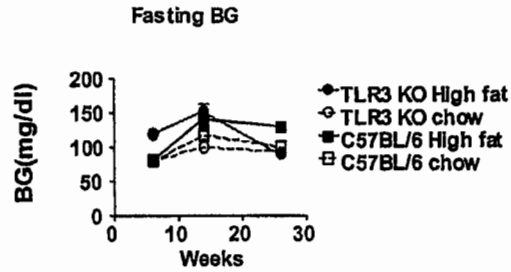

Fasting BG
BG(mg/dl)
200
150
100
50
0
0
10
20
30
Weeks
TLR3 KO High fat
TLR3 KO chow
C57BL/6 High fat
C57BL/6 chow

Figure 33A

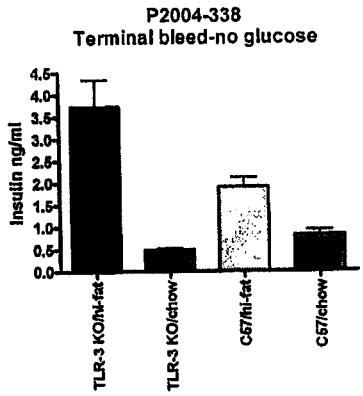


Figure 33B

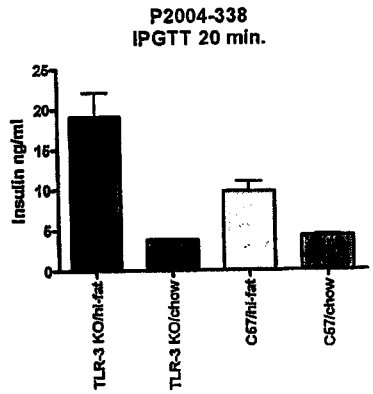


Figure 33C

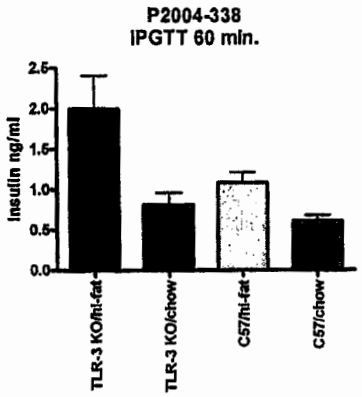

P2004-338
IPGTT 60 min.
Insulin ng/ml
2.5
2.0
1.5
1.0
0.5
0.0
TLR-3 KO/hi-fat
TLR-3 KO/chow
C57/hi-fat
C57/chow

Figure 34A

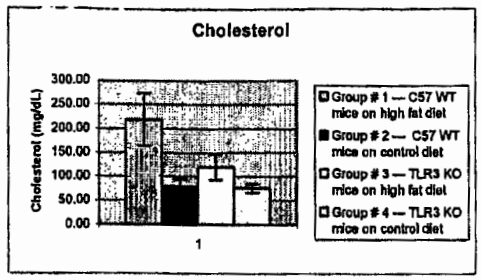


Figure 34B

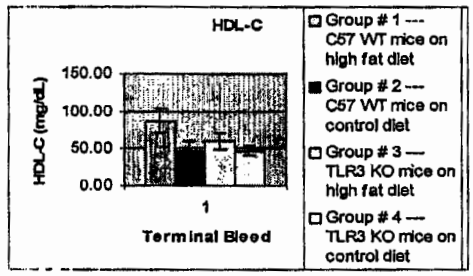


Figure 34C

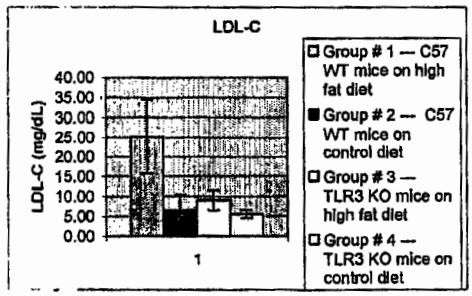


Figure 34D

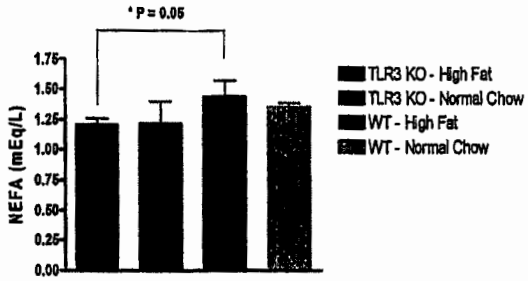


Figure 34E

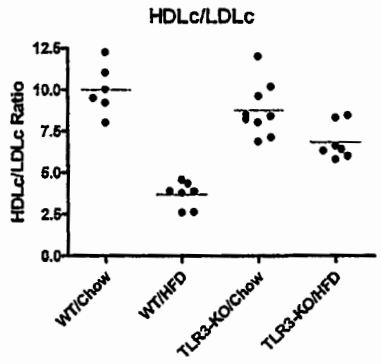


Figure 35

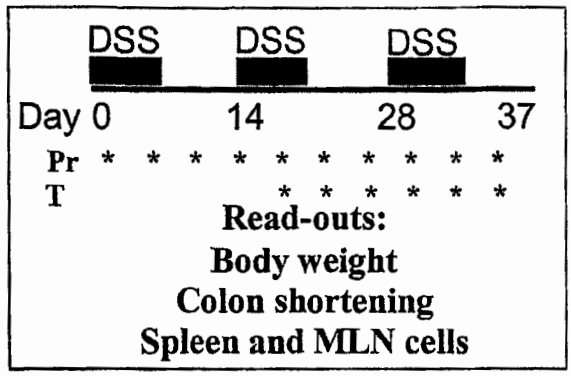

DSS
DSS
DSS
Day 0
14
28
37
Pr * * * * * * * * * *
T * * * * * *
Read-outs:
Body weight
Colon shortening
Spleen and MLN cells

Figure 36

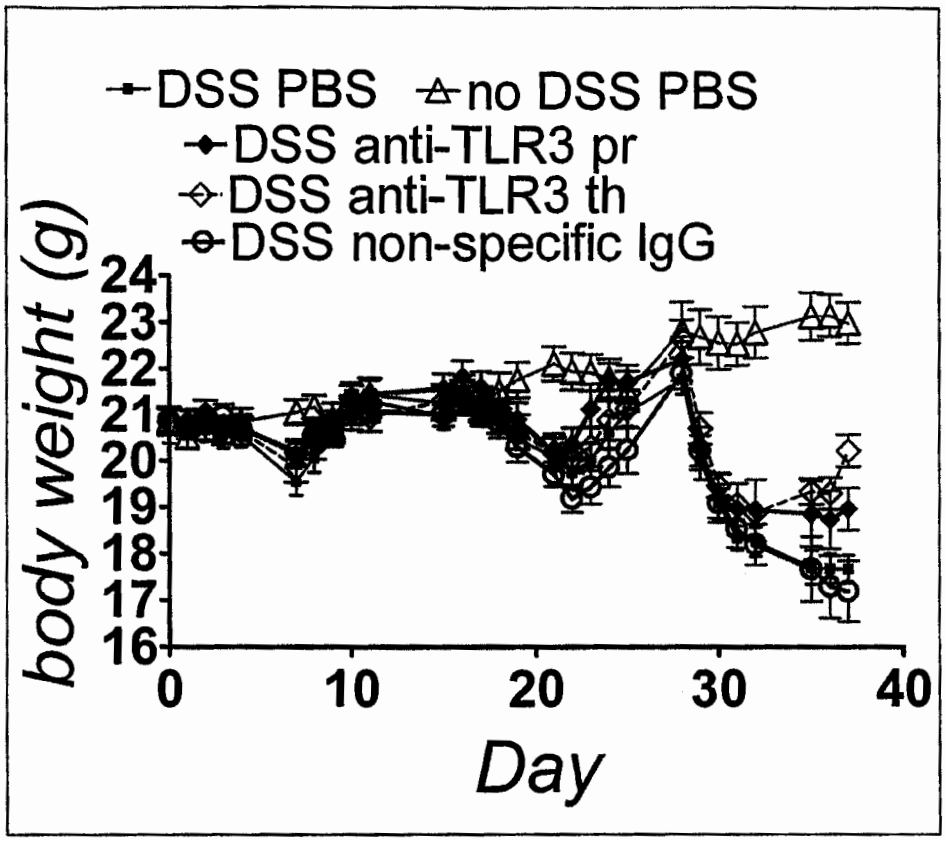

DSS PBS
no DSS PBS
DSS anti-TLR3 pr
DSS anti-TLR3 th
DSS non-specific IgG
body weight (g)
24
23
22
21
20
19
18
17
16
0
10
20
30
40
Day

Figure 37

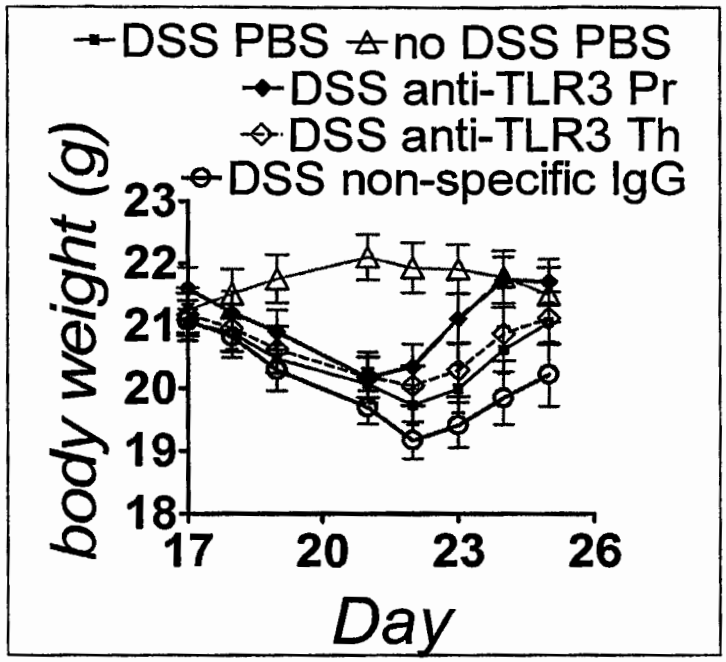

DSS PBS
no DSS PBS
DSS anti-TLR3 Pr
DSS anti-TLR3 Th
DSS non-specific IgG
body weight (g)
23
22
21
20
19
18
17
20
23
26
Day

Figure 38

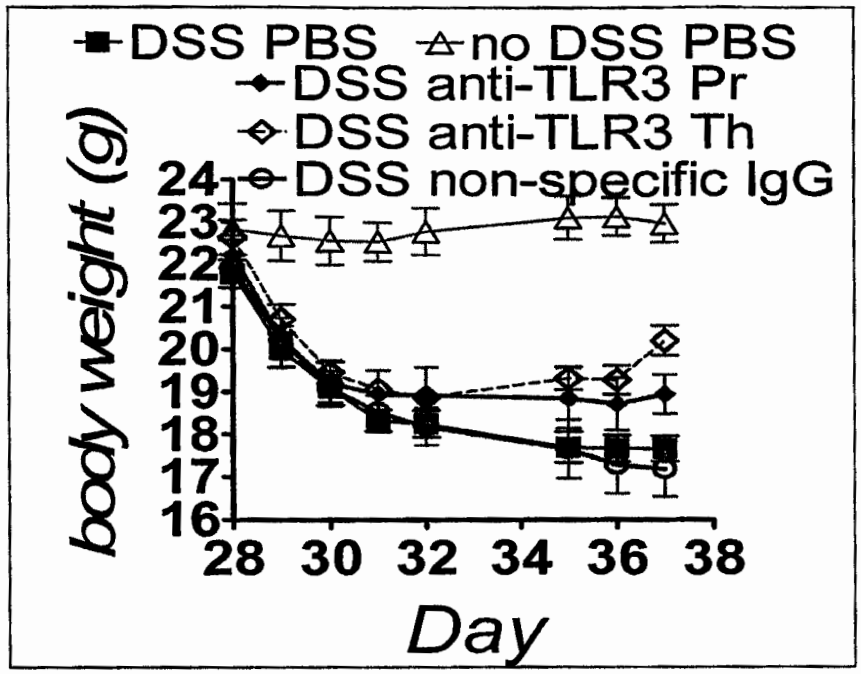

DSS PBS
no DSS PBS
DSS anti-TLR3 Pr
DSS anti-TLR3 Th
DSS non-specific IgG
body weight (g)
24
23
22
21
20
19
18
17
16
28
30
32
34
36
38
Day

Figure 39

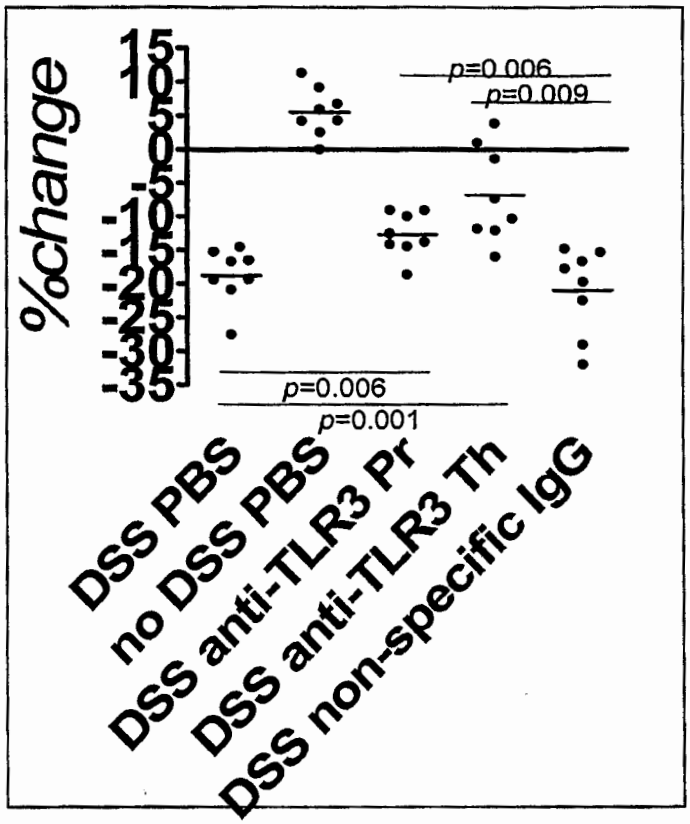

%change
15
p=0.006
p=0.009
p=0.006
p=0.001
DSS PBS
no DSS PBS
DSS anti-TLR3 Pr
DSS anti-TLR3 Th
DSS non-specific IgG

Figure 40

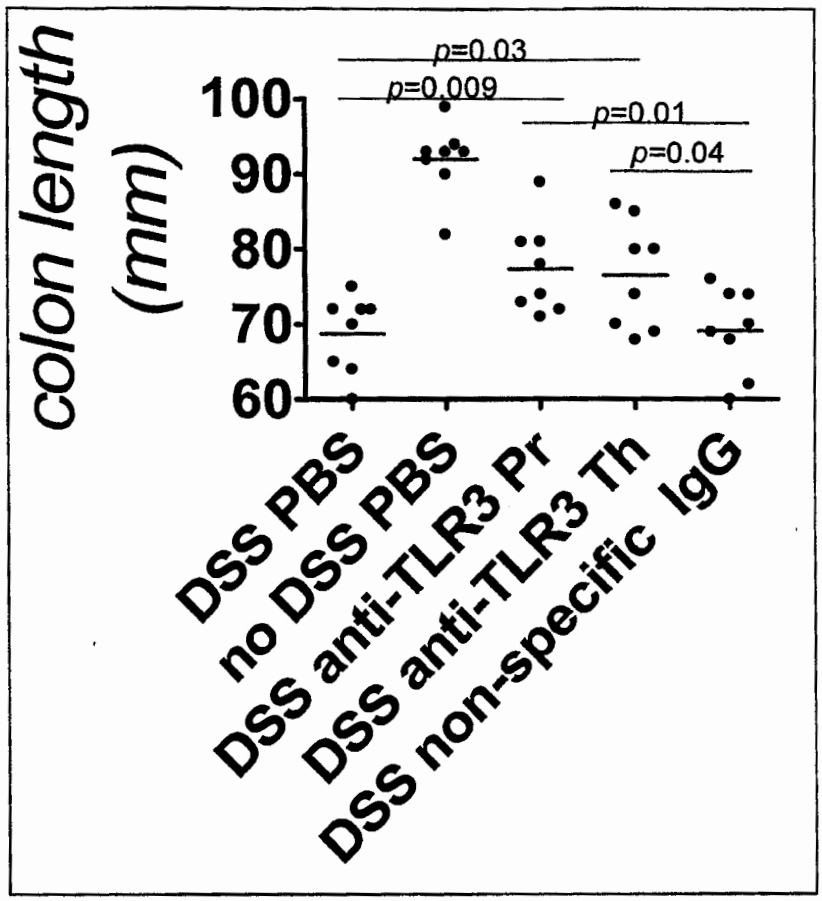

colon length (mm)
100
90
80
70
60
p=0.03
p=0.009
p=0.01
p=0.04
DSS PBS
no DSS PBS
DSS anti-TLR3 Pr
DSS anti-TLR3 Th
DSS non-specific IgG

Figure 41A

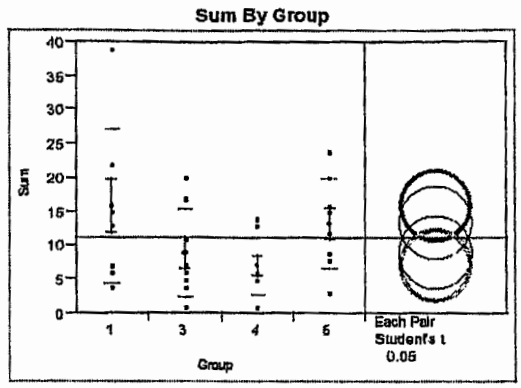


Figure 41B

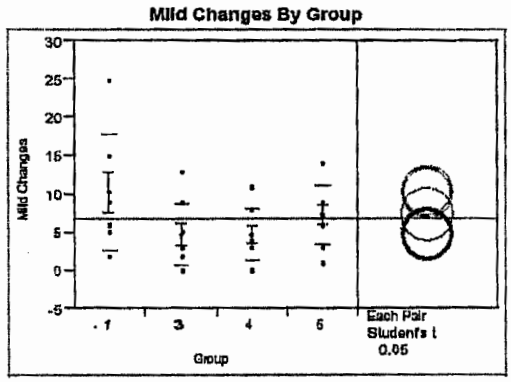


Figure 41C

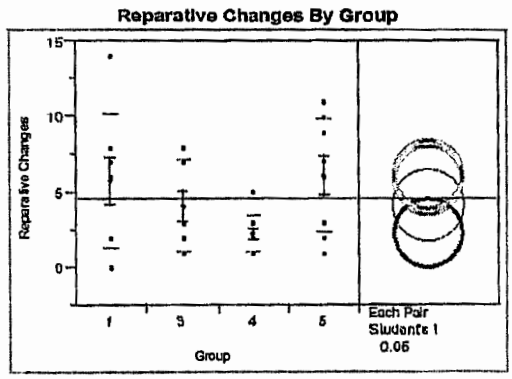


Figure 41D

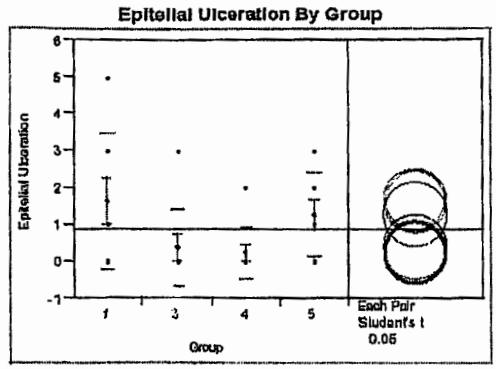


Figure 41E

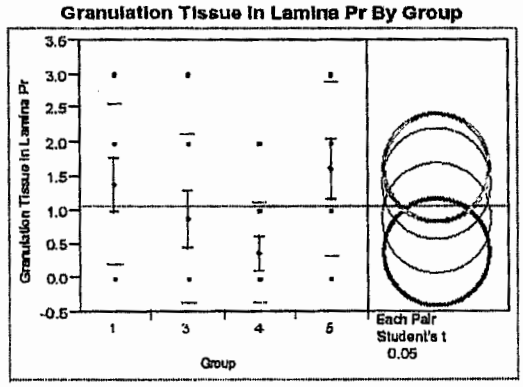


Figure 41F

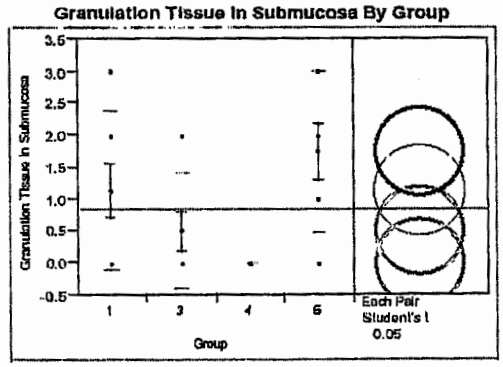


Figure 42

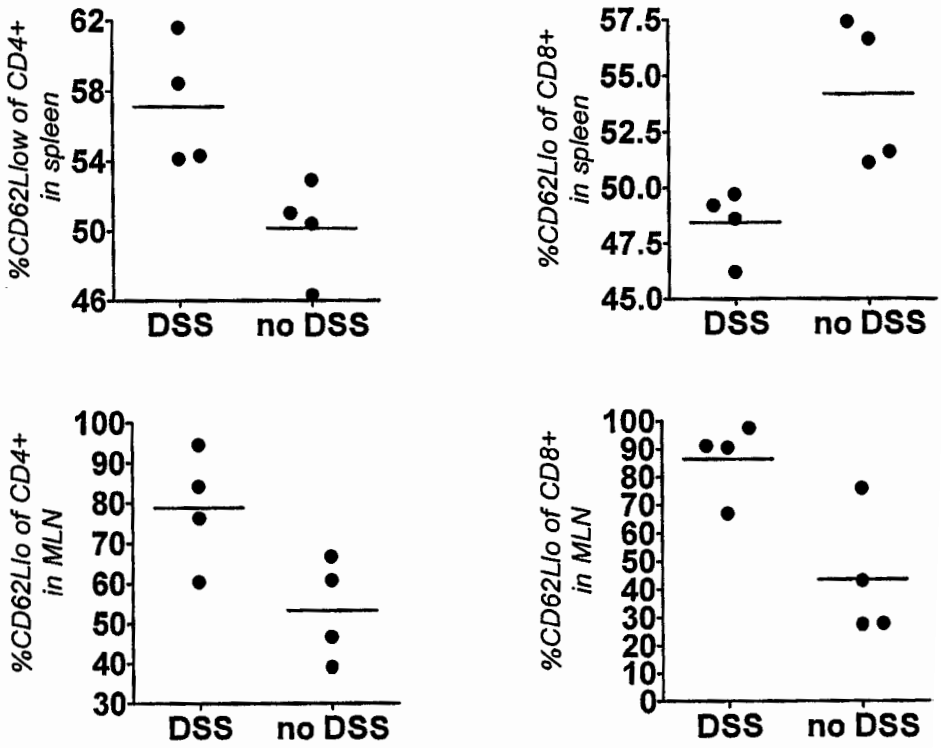

%CD62Llow of CD4+ in spleen
62
58
54
50
46
DSS
no DSS
%CD62Llo of CD8+ in spleen
57.5
55.0
52.5
50.0
47.5
45.0
DSS
no DSS
%CD62Llo of CD4+ in MLN
100
90
80
70
60
50
40
30
DSS
no DSS
%CD62Llo of CD8+ in MLN
100
90
80
70
60
50
40
30
20
10
0
DSS
no DSS

Figure 43

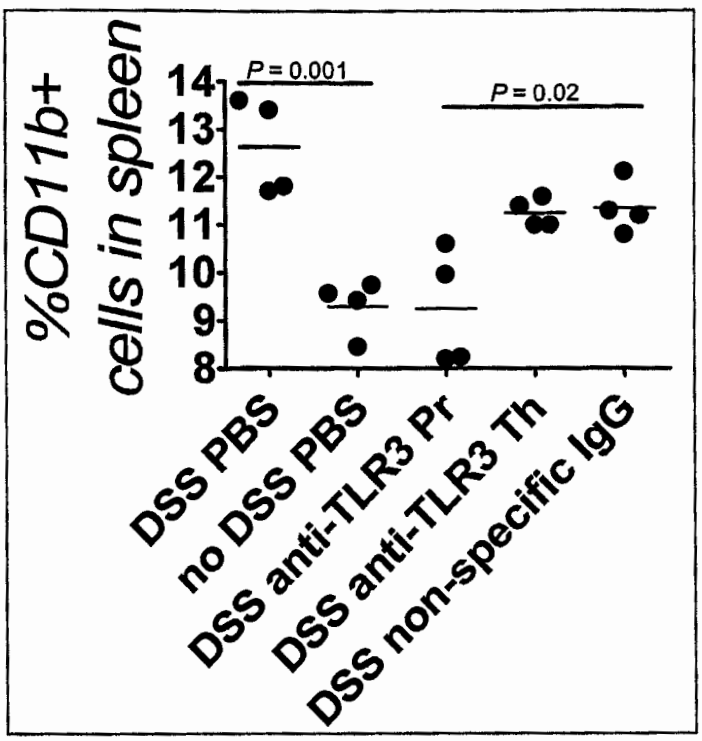
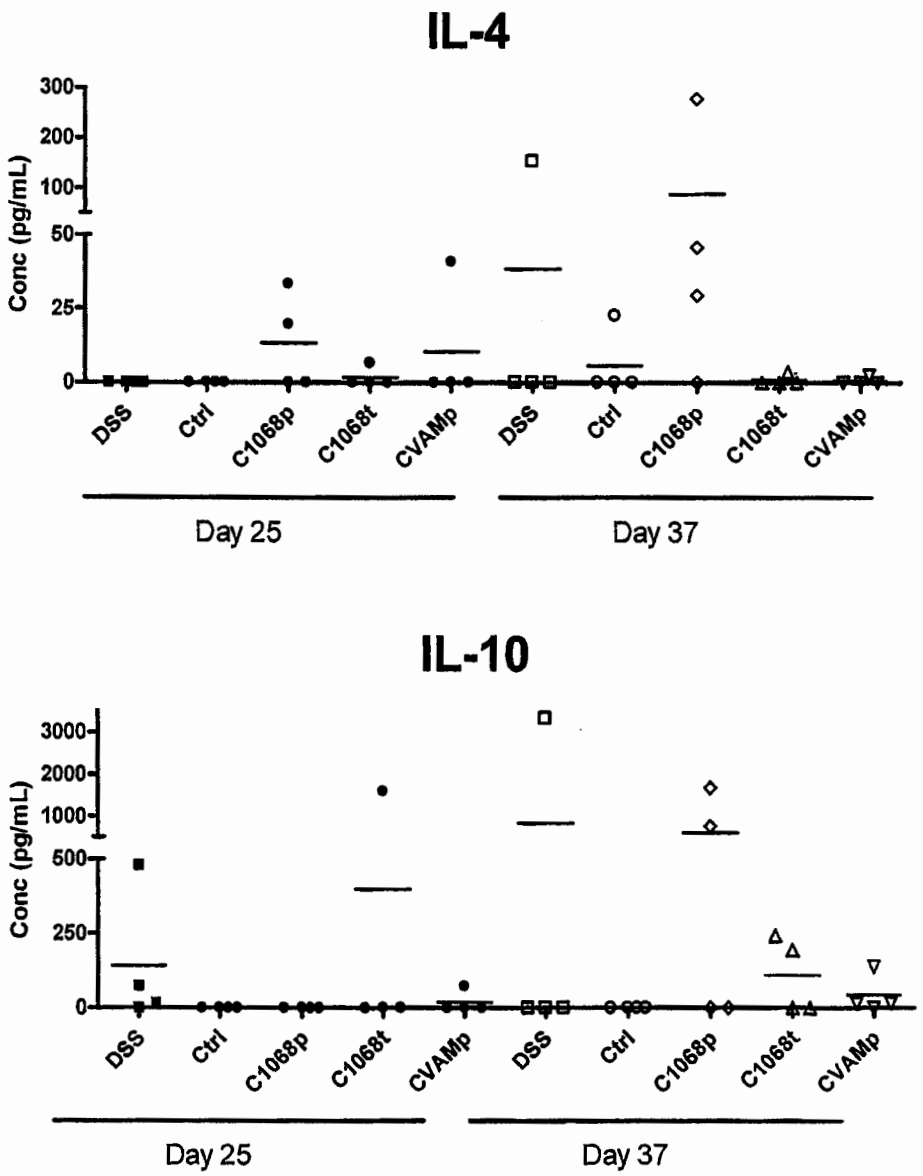

%CD11b+ cells in spleen
14
13
12
11
10
9
8
P = 0.001
P = 0.02
DSS PBS
no DSS PBS
DSS anti-TLR3 Pr
DSS anti-TLR3 Th
DSS non-specific IgG

Figure 44


IL-4
Conc (pg/mL)
300
200
100
50
25
0
DSS
Ctrl
C1068p
C1068t
CVAMp
DSS
Ctrl
C1068p
C1068t
CVAMp
Day 25
Day 37
IL-10
Conc (pg/mL)
3000
2000
1000
500
250
0
DSS
Ctrl
C1068p
C1068t
CVAMp
DSS
Ctrl
C1068p
C1068t
CVAMp
Day 25
Day 37